SEDATION SOLUTIONS

HIV and sedation 1

Introduction

Bill Clinton said, “We live in a completely interdependent world, which simply means we cannot escape each other. How we respond to AIDS depends, in part, on whether we understand this interdependence. It is not someone else’s problem. This is everybody’s problem”.

A sedation practitioner may see HIV positive patients on any sedation list. It is therefore necessary that we have a basic working knowledge of HIV, as well as its common complications and treatment, especially where it will affect our sedation management. This will help us to make a decision whether we want to do the patient in the surgery or a facility or rather in a hospital environment.

Another important aspect is to protect us from exposure, and to follow the correct procedure in terms of post exposure prophylaxis in the event of a needle stick.

According to the UNAIDS report on global AIDS epidemic 2013, there are 35,3 (32,2 -38,8) million people globally living with HIV. (1)

The basics of HIV (a summary)

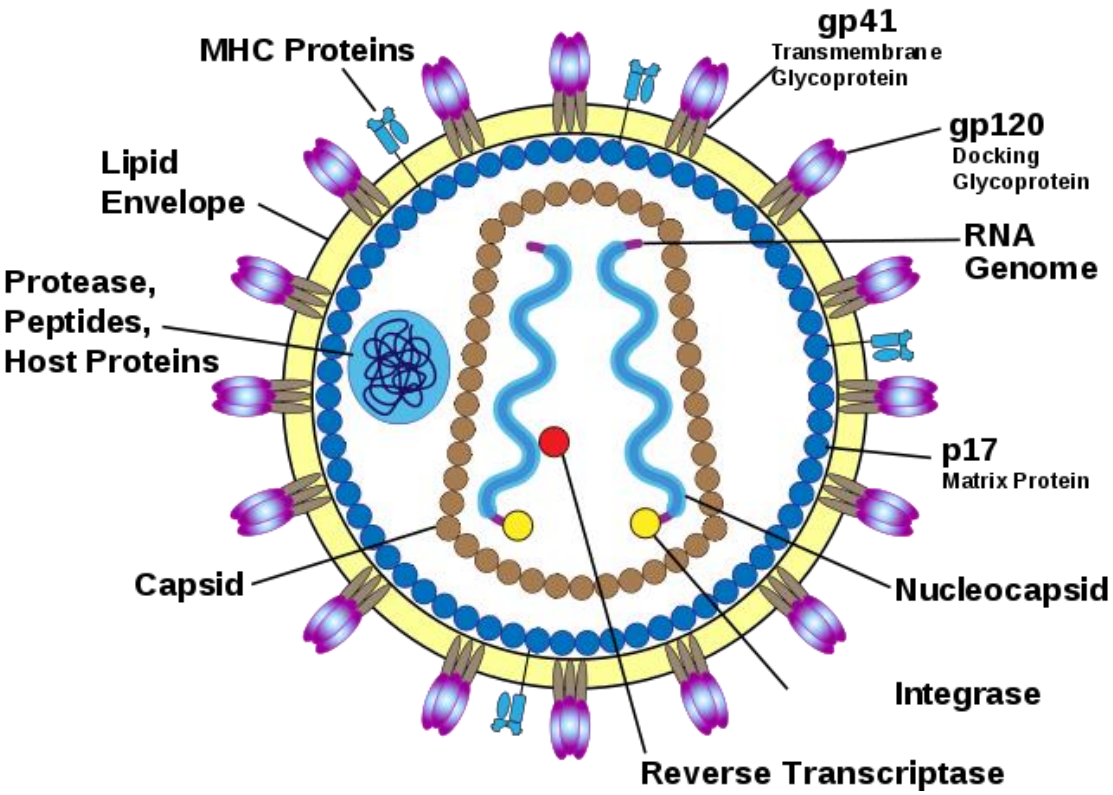
The human immunodeficiency virus (more commonly referred to as HIV) was discovered in 1983 and subsequently found to be the cause of the acquired immune deficiency syndrome (AIDS). HIV falls under the family Retroviridae and the genus Lentiviridae. As a retrovirus HIV does not contain DNA and has only RNA.

For HIV to replicate, it needs the enzyme reverse transcriptase, which is an RNA-dependent DNA polymerase that has the function of transcribing RNA into DNA. This reverse transcriptase enzyme is only found in viruses and not in humans.

HIV gains entry into the CD4+ cells in humans where it replicates and matures. Two main subtypes exist namely HIV-1 (most common worldwide) and HIV-2 (less common with a slower progression).

SEDATION SOLUTIONS

Structure of HIV



HIV consists of an outer lipid envelope that is composed of a lipid bilayer derived from the host, as the HIV cell breaks free from the CD4+cell. It also contains two single strands of HIV RNA: the RNA genome. Viral enzymes within the core are reverse transcriptase, protease and integrase.

The p24 capsid protein that surrounds the inner core of the HIV can be used very early in the disease progression to detect p24 antigen levels in the blood. Proteins gp120 and gp41 are located inside the lipid envelope.

Binding of the virus to the CD4+ cell

Gp120 (the docking glycoprotein) binds HIV to the CD4+ cell membrane.

A change in the HIV conformation then exposes gp41 (trans membrane glycoprotein), which allows the virus to bind with the chemokine co-receptors (CCR5 or CXCR4) on the CD4+ cell. Fusion of the virus to CCR5 or CXCR4 allows the virus to gain entry to the host CD4+ cell through a pore.

ONCE INSIDE THE CD4+ CELL

The two enzymes reverse transcriptase and viral integrase are responsible for the replication of the virus. HIV reverse transcriptase transcribes the single-stranded HIV RNA into the double-stranded HIV DNA. Viral integrase then integrates the double strand of HIV RNA into the DNA of the host. In the nucleus of the host cell the HIV DNA is transcripted to HIV-messenger RNA. (mRNA). The mRNA then gets translated into polypeptide chains of HIV precursor proteins.

Viral protease cleaves these polypeptide chains to form a new viral core and thus is important in the maturation of the virus. As the core breaks through the host's cell wall, it takes with it a part of the host's cell membrane to form the outer lipid envelope and voila! A new HIV viral particle is formed. The maturation process driven by viral protease is an important step and without it, the released virus is not infectious to other CD4+ cells.

Clinical staging of HIV (2)

Stage	Associated symptoms
1	Asymptomatic Persistent lymphadenopathy that is generalized
2	Mild symptoms: Moderate weight loss (<10% body weight) Recurrent upper respiratory tract infections Viral or fungal skin infection Oral or skin lesions

3	Advanced symptoms: Severe weight loss (>10% body weight) Chronic diarrhoea Persistent fever Oral lesions or candidiasis Pulmonary tuberculosis Severe bacterial infections Anaemia, neutropenia, thrombocytopenia
4	Severe symptoms: Wasting “syndrome” AIDS (weight loss >10% body weight with wasting or BMI <18.5) Chronic diarrhoea Persistent fever Encephalopathy, nephropathy, cardiomyopathy Recurrent bacterial infections Malignancy

Complications of HIV

The respiratory system

HIV disease can involve the upper as well as the lower airway. This is very important for the sedation practitioner to know.
The sedation practitioner needs to take possible airway compromise into account with the pre-sedation evaluation and during sedation.

The following respiratory complications can be seen:

- Airway obstruction (Kaposi's sarcoma in the mouth and upper airway may pose a serious challenge for the sedation practitioner to manage the airway)
- Bronchitis
- Sinusitis

- Lymphoma
- Pneumonia
  - Pneumocystis carinii pneumonia
  - Bacterial pneumonia (Streptococcus pneumoniae, Haemophilus influenzae, Staphylococcus aureus and Pseudomonas aeuruginosa
- Pneumonitis
- Tuberculosis, and other mycobacteria and fungal infections

The cardiovascular system

HIV disease may lead to serious pathology of the cardiovascular system that the sedation practitioner needs to evaluate with the pre-sedation evaluation. Cardiovascular disease may be the result of the HIV infection itself or due to the side effects of ARV drugs, chemotherapy or anti-infective agents.

Some important and commonly presenting cardiovascular complications include:

- Acute coronary syndrome
- Cardiomyopathy
- Endocarditis (could be caused by opportunistic bacterial infections which could result in congestive cardiac failure)
- Valve lesions
- Pericardial effusions
- Pulmonary hypertension
- Myocarditis, progressing to cardiomyopathy, can be caused by Cryptococcus, Coxsackie B virus, or Aspergillus infections, as well as lymphoma.

The gastrointestinal system

Some commonly presenting complications of the gastrointestinal system due to HIV infection and its treatment may include:

- Oral and pharyngeal candidiasis that leads to difficulty or pain on swallowing
- Diarrhoea (due to Cryptosporidium infections) with associated electrolyte abnormalities and even dehydration

- Vomiting and loss of appetite
- Increased gastric emptying times; this is an important point for the sedation practitioner as far as fasting is concerned
- Bleeding tendency on airway instrumentation/nasogastric tube insertion
- Diarrhoea with associated electrolyte dysfunction and dehydration
- Liver disease, again important for us as sedation practitioners as many drugs we use are metabolized by the liver
- Pancreatitis

The neurological system

HIV can affect the nervous system by either causing direct infection, inflammation, demyelination or a degenerative process. It can also be secondary to opportunistic infections or malignancies. All structures may be involved including the meninges, brain, spinal cord, peripheral nerve or muscle.

Common complications are:

- Neurocognitive impairment like HIV-related dementia (which could have implications for consent)
- Encephalopathy
- Autonomic neuropathy or polyneuropathy
- Seizures
- Meningitis
- Non-viral infections, e.g. toxoplasmosis, Cryptococcus, Candida, mycobacteria, Treponema and Aspergillus

The renal system

HIV can be associated with acute and chronic renal disease and the causes can be multifactorial:

- Drug-induced nephrotoxicity, hypertension and diabetes

- HIV-associated nephropathy.

These potential complications make it imperative to avoid nephrotoxic drugs and to adjust the dose of drugs excreted by the kidneys. The patient also needs to be adequately hydrated to avoid further deterioration in kidney function.

The haematological system

Common complications during HIV infection include:

- Anaemia
- Neutropenia
- Thrombocytopenia
- Persistent generalized lymphadenopathy
- Haematological malignancies
- Coagulation abnormalities.

HIV treatment guidelines

A new important development is the recent changes to the standardized national eligibility criteria for starting ART regimens for HIV patients. (3) The changes mean that more people will be started on ART regimens earlier in the disease progress, and thus we will be seeing more patients on ART drugs than in the past. Starting patients on ART entails a lifelong commitment from the patient. If the patient does not adhere to the medical regimen for any reason, it can lead to development of resistance and subsequent treatment failure. The earlier the patient starts on the ART, the greater is the long-term survival with an associated lower morbidity.

Goals of ART are to have an undetectable viral load by 24 weeks, and an improvement and extension in the length and quality of the patient's life.

Standardized national eligibility criteria for starting ART regimens for adults and adolescents

A. Eligible to start Lifelong ART

- CD4 count <350 cells/mm3 irrespective of WHO clinical stage

OR

- Irrespective of CD4 count. All types of TB (In patients with TB drug resistance or sensitive, including extra pulmonary TB)
- WHO stage 3 or 4 irrespective of CD4 count

B. Require fast track (i.e. ART initiation within 7 days of being eligible)

- HIV positive women who are pregnant or breast feeding

  OR

- Patients with low CD4 <200

  OR

- Patients with stage 4 irrespective of CD4 count

  OR

- Patients with TB/HIV co morbidity with CD4 count < 50
  (Patients with Cryptococcus meningitis or TB meningitis (defer ART for 4-6 weeks)

C. Patients with CD4 above 350, not yet eligible for ART

- Transfer to a wellness program for regular follow-up and repeat CD4 testing 6-monthly
- Advise on how to avoid HIV transmission to sexual partners and children
- Initiate INH prophylaxis if asymptomatic for TB
- Provide counseling on nutrition and contraception and do annual pap smear

Classification of antiretroviral drugs (4) (5)

Drug class	Examples
Nucleoside analogue reverse transcriptase inhibitors (NRTIs)	Zidovudine (AZT) Didanosine (ddl) Lamivudine (3TC) Stavudine (d4T) Emtricitabine (FTC) Abacavir (ABC) Elvucitabine Apricitabine
Nucleotide reverse transcriptase inhibitors (NtRTIs)	Tenofovir (TDF)

Nucleoside analogue reverse transcriptase inhibitors (NRTIs)	Zidovudine (AZT) Didanosine (ddl) Lamivudine (3TC) Stavudine (d4T) Emtricitabine (FTC) Abacavir (ABC) Elvucitabine Apricitabine
Nucleotide reverse transcriptase inhibitors (NtRTIs)	Tenofovir (TDF)

Non-nucleoside reverse transcriptase inhibitors (NNRTIs)	**Nevirapine (NVP)** **Efavirenz (EFV)** **Delavirdine (DLV)** **Etravirine**
Protease inhibitors (PIs)	Indinavir (IDV) Ritonavir (RTV) Saquinavir (SQV) Nelfinavir (NFV) Lopinavir (LPV) Tiprinavir Darunavir Atazanavir
Fusion inhibitors	Enfuvirtide (T-20)
CCR5 co-receptor antagonists	Maraviroc Vicriviroc
Integrase inhibitors	Raltegravir Elvitegravir
Maturation inhibitors	Beviramat

Discussion

The above is in effect an introduction to our article on HIV and sedation. It is clear that many drugs are available for treatment and prevention of HIV. The sedation practitioner must be aware of all these drugs that are available as they may influence the sedation process. In the article to follow we will cover,

- Mechanism of action of antiretroviral drugs
- Their side-effects and significance for the sedation practitioner
- Drug interactions
- Drugs that are safe to use for sedation in HIV positive patients
- Impact of sedation drugs on the immune system and HIV
- Approach to a HIV positive patient for sedation
- Fasting and antiretroviral drugs
- Risks involved for sedation practitioners
- Correct procedure after occupational exposure
- Ethical responsibilities

It is clear from what we have discussed that HIV may be a multi-organ disease. The sedation practitioner needs to do a proper pre-sedation evaluation and look for any complications of the disease. The medical history questionnaire will be valuable to help the sedation practitioner to assess the condition of the patient.

An important decision would be, does the HIV positive patient qualify for sedation outside the hospital setting. We have to decide whether we can classify our patient as an ASA 11 patient. The above information will be helpful to make a decision as to where to do the sedation and the operation.

I want to recognize the contribution of Theresa Samuels to this article.

SEDATION SOLUTIONS

References

1. Global report: UNAIDS report on global AIDS epidemic 2013. Available from: http://www.unaids.org/en/media/unaids/contentassets/documents/epidemiology/2013/gr2013/UNAIDS_Global_Report_2013_en.pdf

2. Wilson S. HIV and anaesthesia. Update in anaesthesia. Available from: http://update.anaesthesiologists.org/wp-content/uploads/2009/10/HIV-and-Anaesthesia.pdf

3. Department of Health: The South African antiretroviral treatment guidelines 2013. Published 24 March 2013 Available from: http://www.doh.gov.za/docs/policy/2013/ART_Treatment_Guidelines_Final_25March2013.pdf

4. Milner A, Welch E. Applied pharmacology in anaesthesiology and critical care: Chapter 19 Antiretroviral agents by Piercy, JL. 1st edition. South Africa: Medpharm publications (PTY LTD) 2012:page 628-654

5. Chemotherapy of HIV infection. South African Medicines Formulary, 8th edition. 2008:page 318-329